IRB Review of Bio-repository Research

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Agenda

- Agreeing on the definitions
- Three components of tissue banking
- Regulatory issues and compliance for:
  - The specimen source
  - The bank itself
  - Specimen recipients/users
- Regulatory obstacles

Agreeing on the Definitions

- Tissue
- Bank or repository

Agreeing on the Definitions

- **Tissue**
  - Any biological specimen obtained from patients or research subjects. This includes; for example, fixed, frozen or fresh pathology or autopsy specimens, blood, urine, saliva, CSF, semen, breast milk or other biological material and any purified DNA, RNA, proteins, cell lines.
  - Terms *tissue, specimen and sample* are often used interchangeably.

Agreeing on the Definitions

- **Research Repository or Bank**
  - An entity involved in procuring, processing, storing and/or distributing tissue expressly for research use.

The Three Components of Tissue Banking

Specimen Source

Specimen Source/s

- How will the specimen be obtained?
  - As part of clinical care
  - Specifically for research
- Will the specimen be identifiable?

The answers to these questions determine the regulatory requirements

How will the specimen be obtained?

- Obtained as part of routine clinical care:
  - "Excess" left over after all clinical needs have been completed
    - 10 cc of blood routinely drawn for a clinical test
    - The blood lab only used 8 cc
    - 2 cc are in excess and would otherwise be discarded

How will the specimen be obtained?

- Obtained specifically for research:
  - "Extra" obtained during clinical care
    - 10 cc of blood needed for a clinical test
    - 15 cc drawn to provide 5 cc for research
  - Procedure performed solely for research
    - No blood needed for clinical care
      - Venapuncture performed solely to obtain 5 cc of blood for research

Will the specimen be identifiable?

- Will the specimen be maintained with any identifiable information?
  - Direct identifiers
  - Coded information with access to a link to the code
  - Coded information with no access to the link to the code

The Bank Itself

The Bank:
Who 'owns' it/Who runs it

- For-profit or not-for-profit
- Academic Medical Center
- Single vs multiple institutions
- HIPAA covered or not?

The Bank:
What is the Focus?

- Specific disease or condition
- Any and all available specimens
- Clinical and/or research specimens

The Bank: Identifiable or Not-Identifiable

- Will the specimen be maintained with any identifiable information?
  - Direct identifiers
  - Coded information with access to a link to the code
  - Coded information with no access to a link to the code

How are Specimens Handled? Does the Bank:

- Process specimens in any way
- Validate the diagnosis
- Update clinical information related to the specimen
- Expect to receive results of any research that utilized the Bank's specimens

How does the Bank allocate specimens?

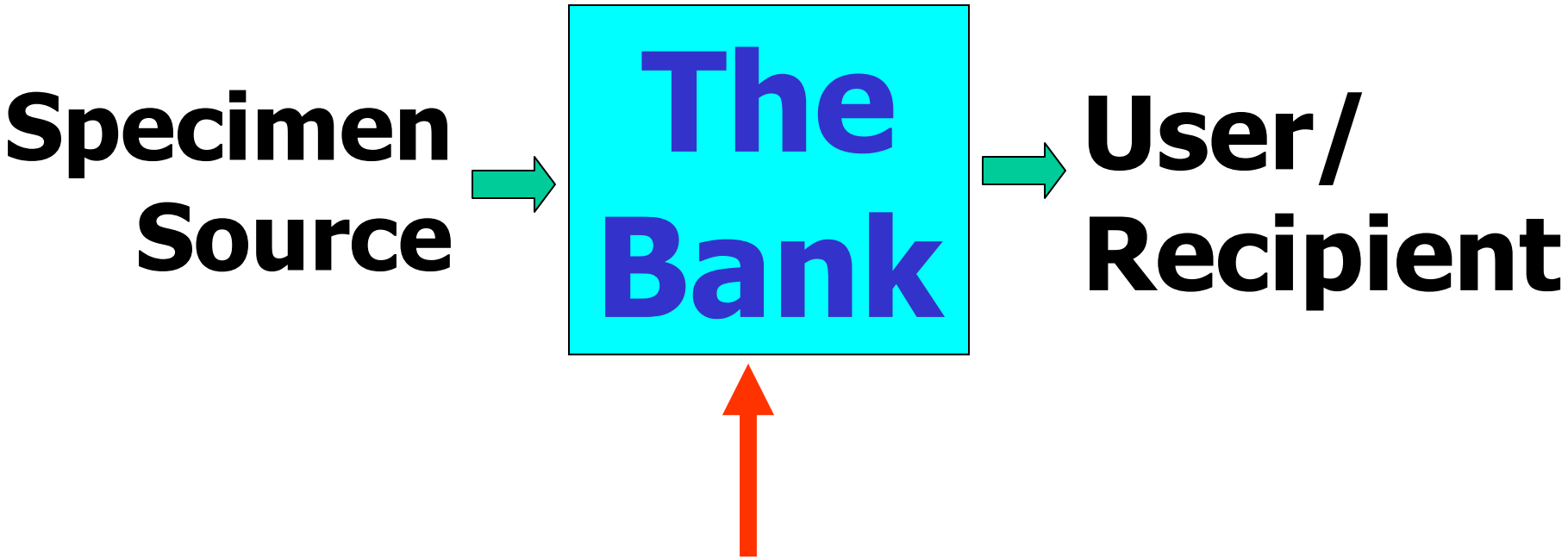
- Does the bank have 'rules?'
  - Can anyone receive specimens?
  - Are there eligibility criteria?
- Does the bank provide identifiable specimens?
- How does the bank process requests?

Specimen Recipients/Users

Specimen Recipients/Users

- Can you obtain identifiable specimens?
- Can you obtain updated clinical information?
- Are you expected to share any research results with the bank?

How the Regulations apply


Specimen Source
The Bank
User/ Recipient
How the Regulations apply

The Bank: IRB Review

- The Bank itself is considered a research protocol
- Review of all processes for:
  - Intake of specimens
  - Maintenance of specimens in bank
  - Processing (if any) of specimens in bank
  - Output of specimens to requesting researchers

The Bank: IRB Review
Intake of Specimens

- Consent issues:
  - Who obtains consent
  - Who ascertains that all elements are included
- Quality of specimens
  - How is diagnosis and quality of specimen assessed

The Bank: IRB Review

Maintenance of Specimens in Bank

- Who is in charge of the physical storage procedures
- How is privacy protected
- If future clinical data is collected how is this done
- If a subject withdraws consent, how is this processed

The Bank: IRB Review

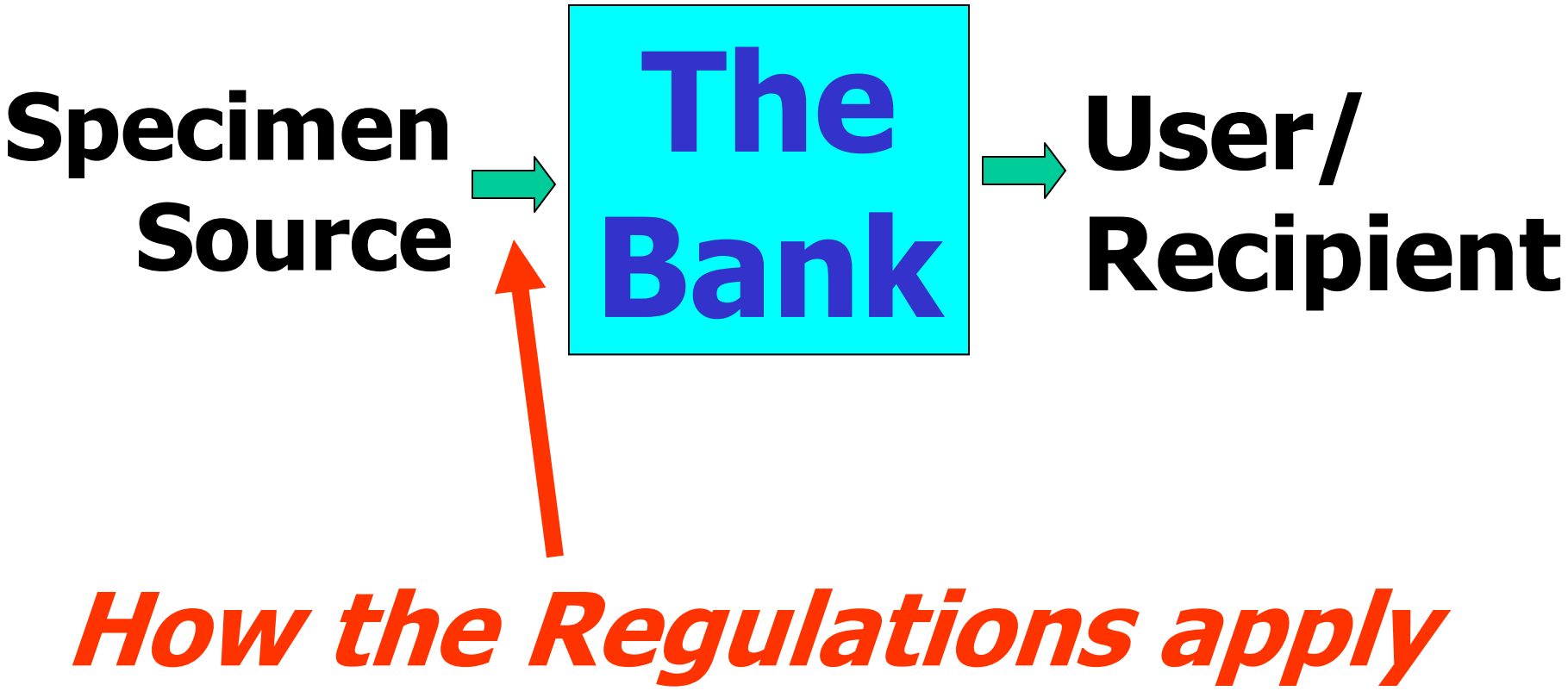
Processing of Specimens in Bank

- If physically processed: by whom
- If identifiable specimens are:
  - Anonymized – by whom
  - Coded – by whom and who keeps the code

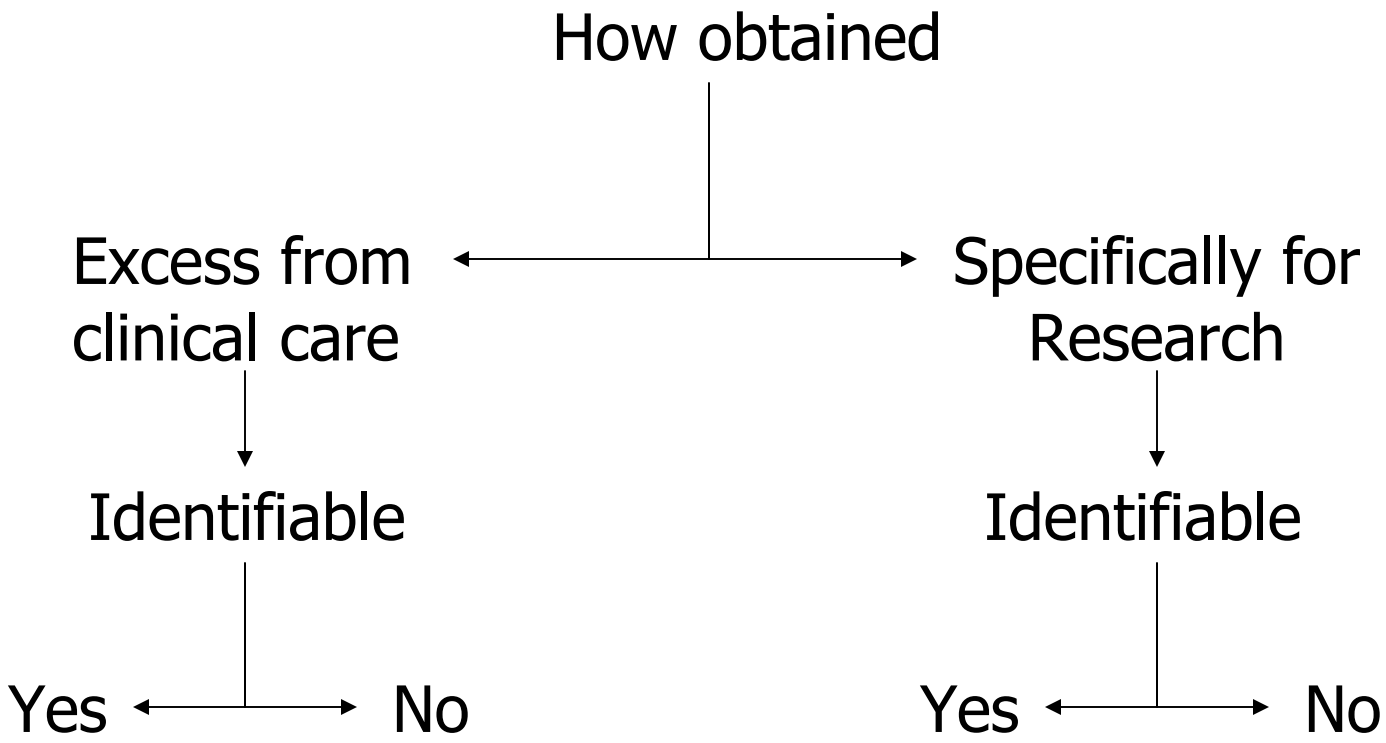
The Bank: IRB Review

Output of Specimens from Bank

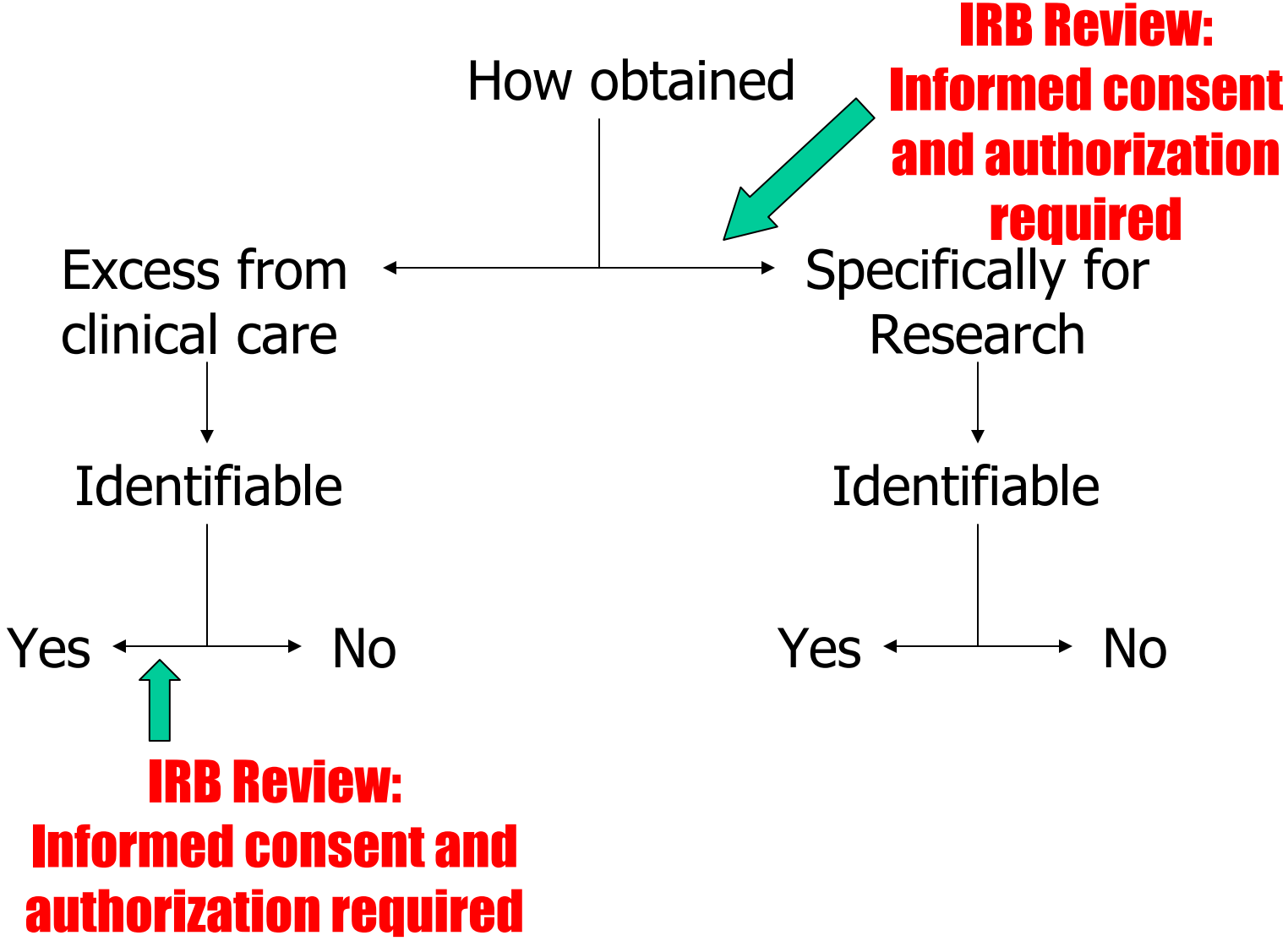
- Who processes requests
- Who ascertains adequacy of informed consent and authorization
- Are there restrictions re:
  - Who can access specimens


Specimen Source
The Bank
User/ Recipient
How the Regulations apply

Specimen Source



Specimen Source



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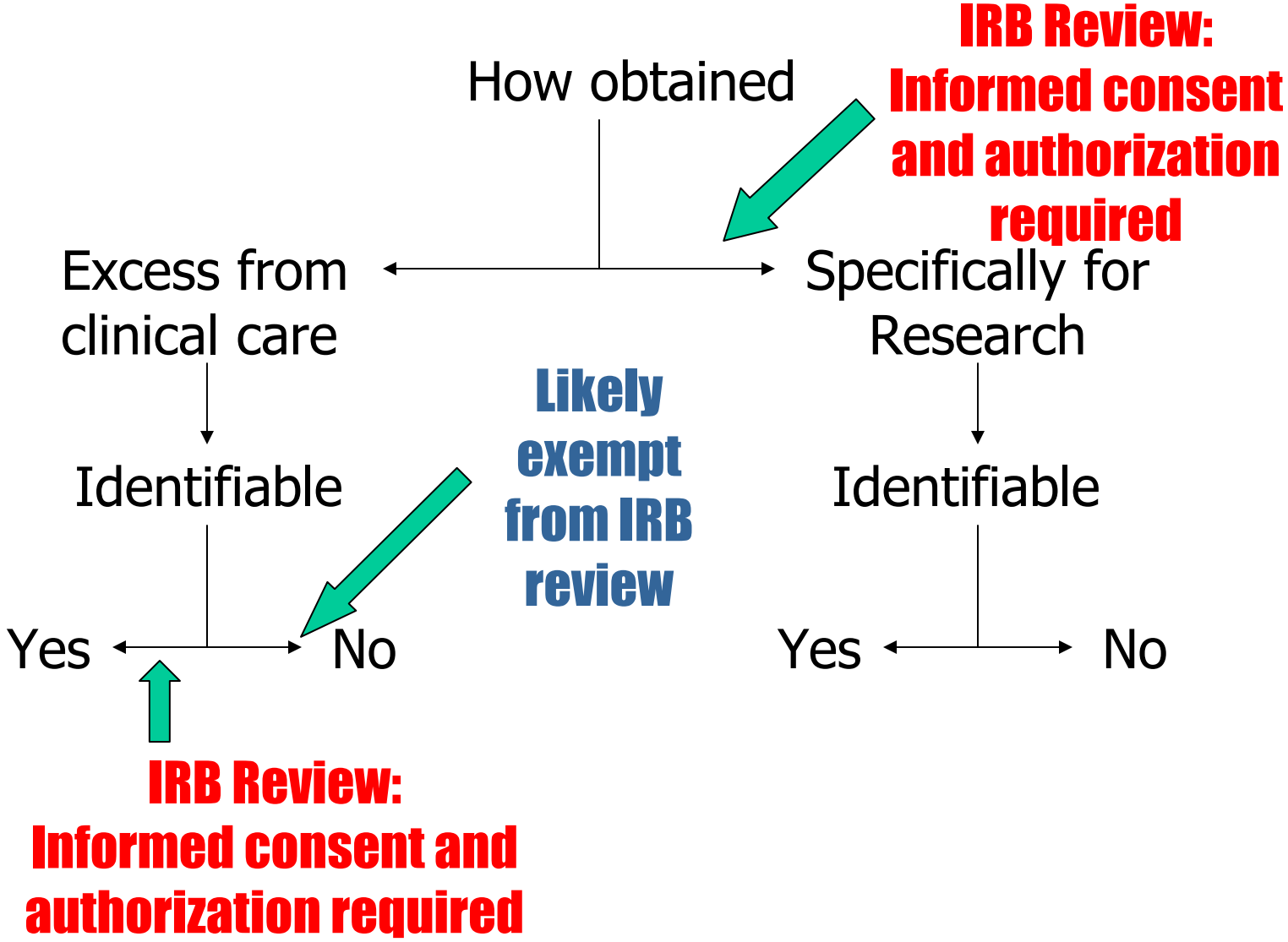


Not involving human subjects:

Research involving only coded private information or specimens if:

- Not collected specifically for this research project via interaction with living individuals; and
- Investigators cannot readily ascertain the identity because, for example:
  - Key to code is destroyed prior to research
  - Investigator and holder of identifiers enter into an agreement prohibiting release of identifiers to investigators*
  - IRB-approved repository written policies and operating procedures that prohibit the release of identifiers to the investigators*, or
  - Other legal requirements prohibiting the release of identifiers*

* Until the individuals are deceased

Depositing into the Bank
Informed Consent

- Details of how the bank operates
- How specimens will be maintained in the bank
- How specimens will be used
  - Limited use?
  - Un-restricted use?
- Who will have access to the specimens

Depositing into the Bank
Informed Consent

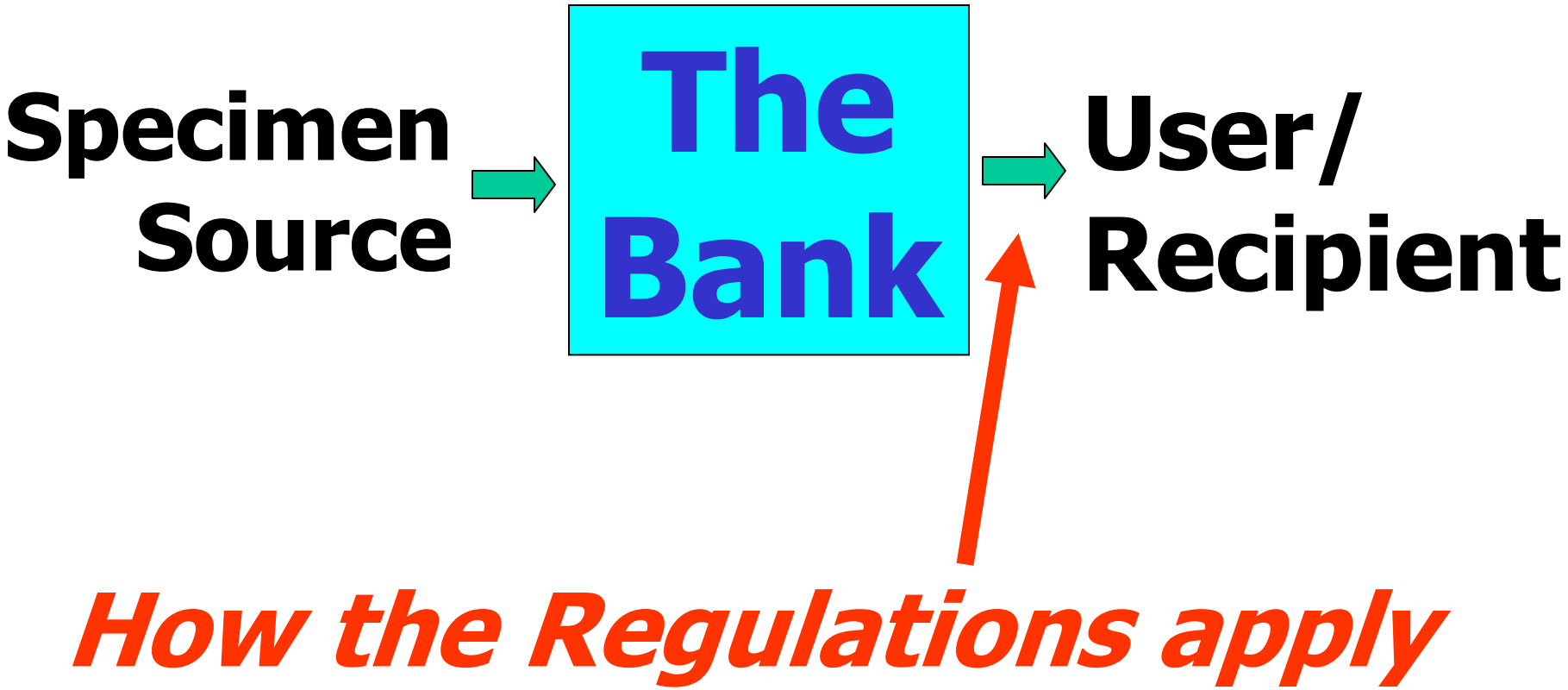
- How identifiers will be protected
- Whether or not bank employees will access medical records in the future
- If subjects will ever be re-contacted for future consent
  - To provide additional specimens
  - To provide additional information
  - To provide consent for additional specimen uses

Depositing into the Bank
Informed Consent

- If subject will ever know how their specimen was used
- If subject will/can receive research results
- How subject can withdraw their specimen from the bank

Privacy Rule Concerns

- If the bank is a HIPAA entity
  - Deposits of identifiable specimens into the bank require authorization or waiver
  - Withdrawal of identifiable specimens from the bank requires authorization or waiver
    - N.b., if a waiver, disclosure must be tracked


Specimen Source
The Bank
User/ Recipient
How the Regulations apply

IRB Review for Recipient

- IRB review required for use of any identifiable specimens
  - If the use is covered in the initial IRB review and consent for placement into the bank, a second review is not required
  - If the use is not covered in the initial IRB review and consent, a new IRB review is required

Recipient: Example 1

- Investigator requests 10 identifiable liver biopsy samples for the purpose of studying alcoholic cirrhosis:
  - When specimens were placed in the bank, all donors signed a consent form that described:
    - Future uses for the study of any liver disease
    - Future uses limited to cancer research

IRB Review for Recipient

- IRB review may be required for use of non-identifiable specimens
  - If the use is covered in the initial IRB review, a second review is not required
  - If the use is not covered in the initial IRB review, a new IRB review is required

Recipient: Example 2a

- Investigator requests 10 non-identifiable liver biopsy samples for the purpose of studying alcoholic cirrhosis:
  - All specimens were obtained as research specimens, and all donors signed a consent form that described:
    - Future uses for the study of any liver disease
    - Future uses limited to cancer research

Recipient: Example 2b

- Investigator requests 10 non-identifiable liver biopsy samples for the purpose of studying alcoholic cirrhosis:
  - All specimens were anonymous clinical specimens to be discarded, there was no consent obtained

Regulatory Inconsistencies

Regulatory Inconsistencies

- Who/what the specific regulation covers
- Definition of 'identifiable'
- Ability to obtain consent for future unspecified research
- Ability to grant a waiver of permission

Regulatory Inconsistencies

- **Who/What the specific regulation cover**
  - Common Rule: covers live subjects: coverage hinges on funding source
  - FDA regulations: coverage hinges on whether the activity is regulated by the FDA
  - Privacy Rule: covers protected health information within a covered entity. Covers live and deceased persons

Regulatory Inconsistencies

- **Definition of 'identifiable'**
  - Privacy Rule: most expansive definition – specific listing of 18 elements
  - Common Rule: 'readily identifiable'
  - FDA Regulations: does not define

Regulatory Inconsistencies

- **Ability to obtain consent for future unspecified research**
  - Common Rule and FDA regulations allow permission for future unspecified uses
  - Privacy Rule requires specificity of the authorization

Regulatory Inconsistencies

- **Ability to grant a waiver of permission**
  - Common Rule and Privacy Rule allow an IRB/Privacy Board to approve a waiver of consent/authorization if certain conditions are met
  - FDA regulations do not allow a waiver of informed consent
    - N.b. new guidance

References

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